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Patterns of DNMT1 Promoter Methylation in Patients with Acute Lymphoblastic Leukemia

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ABSTRACT

Background: Acute lymphoblastic leukemia (ALL) is a clonal malignant disorder characterized by an uncontrolled proliferation of immature T or B lymphocytes. Extensive studies have shown that the epigenetic changes, especially modified DNA methylation patterns in the regulatory regions through the DNA methyltransferase (DNMTs), play an important role in the development of genetic disorders and abnormal growth and maturation capacity of leukemic stem cells (LSCs).The aim of this study was to evaluate the changes in DNMT1 promoter methylation and its expression pattern in patients with ALL.

Subjects and Methods: In this experimental study, methylation specific PCR (MSP) was used to assess the methylation status of DNMT1 promoter regions in samples collected from ALL patients (n=45) and healthy control subjects. According to this method, un-methylated cytosine nucleotides are converted to uracil by sodium bisulfite and the proliferation of methylated and un-methylated regions are performed using specific primers for target sequences.

Results: None of the patients with B and T-ALL showed methylated promoter regions of the DNMT1 gene, while the methylation pattern of both pre-B ALL patients and the control group showed a relative promoter methylation.

Conclusion: Analysis of promoter methylation patterns in various subgroups of ALL has revealed the importance of DNMT1 in the regulation of gene expression. Likewise, extensive data have also highlighted the methylation-based mechanisms exerted by DNAM1 as one of the main participants regulating gene expression in B-ALL and T-ALL patients. Investigation of the overall DNA methylation pattern offers significant improvements in the prediction of disease prognosis and treatment response.

Keywords: Acute lymphocytic leukemia, Epigenetic, Methylation, DNA methyltransferase

INTRODUCTION

Acute lymphoblastic leukemia (ALL) is a clonal hematopoietic stem cell disorder, caused by several geneticchanges that increased the production of immature lymphoid cells. It is associated with a wide spectrum of molecular and clinical heterogeneities, as the different types of mutations may increase the risk of developing the disease[1]. Early events through the evolutionary origin of abnormal lymphocytes begin by escaping the normal growth regulation mechanisms and gene defects involved in lymphoid proliferation and